Abstract f the Disclosure

An attenuated strain of *Salmonella typhimurium* has been used as a vehicle for oral genetic immunization. Eukaryotic expression vectors containing the genes for b-galactosidase, or truncated forms of ActA and listeriolysin - two virulence factors of *Listeria monocytogenes* - that were controlled by an eukaryotic promoter have been used to transform a *S. typhimurium aroA* strain. Multiple or even single immunizations with these transformants induced a strong cytotoxic and helper T cell response as well as an excellent antibody response. Multiple immunizations with listeriolysin transformants protected the mice completely against a lethal challenge of *L. monocytogenes*. Partial protection was already observed with a single dose. ActA appeared not to be a protective antigen.

The strength and the kinetics of the response suggested that the heterologous antigens were expressed within the eukaryotic host cells following transfer of plasmid DNA from the bacterial carrier strain. Transfer of plasmid DNA could be unequivocally shown *in vitro* using primary peritoneal macrophages. The demonstration of RNA splice products and expression of β-galactosidase in the presence of tetracycline - an inhibitor of bacterial protein synthesis - indicated that the gene was expressed by host cells rather than bacteria. Oral genetic immunization with *Salmonella* carriers provides a highly versatile system for antigen delivery, represents a potent system to identify candidate protective antigens for vaccination, and will permit efficacious generation of antibodies against virtually any DNA segment encoding an open reading frame.

Add A'